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CLINICAL RESEARCH

Global longitudinal strain software upgrade: Implications for intervendor consistency and longitudinal imaging studies

Amélioration des logiciels permettant d'évaluer le strain longitudinal global : *implications pour la concordance entre vendeurs et pour le suivi longitudinal*

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Echocardiography;
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Summary
Background. — Speckle tracking can be used to measure left ventricular global longitudinal strain (GLS).
Aims. — To study the effect of speckle tracking software product upgrades on GLS values and intervendor consistency.

Abbreviations: 2D, two-dimensional; ASE, American Society of Echocardiography; EACVI, European Association of Cardiovascular Imaging; endo, endocardial; epi, epicardial; GLS, global longitudinal strain; ICC, intraclass correlation coefficient; LOA, limits of agreement; LV, left ventricular; mid, midwall; SD, standard deviation.

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Methods. — Subjects (patients or healthy volunteers) underwent systematic echocardiography with equipment from Philips and GE, without a change in their position. Off-line post-processing for GLS assessment was performed with the former and most recent upgrades from these two vendors (Philips QLAB 9.0 and 10.2; GE EchoPAC 12.1 and 13.1.1). GLS was obtained in three myocardial layers with EchoPAC 13.1.1. Intersoftware and intervendor consistency was assessed. Interobserver variability was tested in a subset of patients.
Results. — Among 73 subjects (65 patients and 8 healthy volunteers), absolute values of GLS were higher with QLAB 10.2 compared with 9.0 (intraclass correlation coefficient [ICC]: 0.88; bias: 2.2%). Agreement between EchoPAC 13.1.1 and 12.1 varied by myocardial layer (13.1.1 only): midwall (ICC: 0.95; bias: −1.1%), endocardium (ICC: 0.93; bias: 1.6%) and epicardial (ICC: 0.80; bias: −3.3%). Although GLS was comparable for QLAB 9.0 versus EchoPAC 12.1 (ICC: 0.95; bias: 0.5%), the agreement was lower between QLAB 10.2 and EchoPAC 13.1.1 endocardial (ICC: 0.91; bias: 1.1%), midwall (ICC: 0.73; bias: 3.9%) and epicardial (ICC: 0.54; bias: 6.0%). Interobserver variability of all software products in a subset of 20 patients was excellent (ICC: 0.97—0.99; bias: −0.8 to 1.0%).
Conclusion. — Upgrades of speckle tracking software may be associated with significant changes in GLS values, which could affect intersoftware and intervendor consistency. This finding has important clinical implications for the longitudinal follow-up of patients with speckle tracking echocardiography.

MOTS CLÉS
Échocardiographie ;
Strain longitudinal ;
Speckle tracking

Résumé
Contexte. — Les possibles modifications des valeurs de *strain longitudinal global* (SLG), induites par les améliorations de version des logiciels, restent inconnues.
Objectifs. — Cette étude avait pour but d'étudier l'impact des upgrades de ces logiciels sur les valeurs de SLG et donc sur la concordance entre constructeurs.
Méthodes. — Des sujets (patients ou sujets sains) ont bénéficié d'une échocardiographie avec acquisition systématique avec des machines de deux constructeurs (Philips et GE), sans modification de position du patient. Le SLG était obtenu en déporté avec les versions anciennes et récentes des logiciels de ces deux constructeurs (Philips QLAB 9.0 et 10.2 ; GE EchoPAC 12.1 et 13.1.1). Le SLG était obtenu sur trois couches myocardiques avec EchoPAC 13.1.1. La concordance entre constructeurs était évaluée avec les deux versions des logiciels de chaque constructeur. La variabilité interobservateur de chaque logiciel était testée sur un échantillon de patients de l'étude.
Résultats. — Parmi 73 sujets (68 patients et 8 sujets sains), le SLG était plus élevé en valeur absolue avec QLAB 10.2 qu'avec 9.0 (coefficient de corrélation intraclasse [CCI] : 0,88 ; biais : 2,2 %). Une bonne concordance était observée entre le SLG à mi-paroi (mid) obtenu à l'aide de l'EchoPAC 13.1.1 et le SLG obtenu à l'aide de l'EchoPAC 12.1 (CCI : 0,95 ; biais : −1,1 %). Le SLG à l'endocarde (endo) obtenu avec EchoPAC 13.1.1 était légèrement plus élevé en valeur absolue que le SLG obtenu avec EchoPAC 12.1 (CCI : 0,93 ; biais : 1,6 %), tandis que le SLG à l'épicarde (épi) obtenu avec EchoPAC 13.1.1 était plus bas en valeur absolue que le SLG obtenu avec EchoPAC 12.1 (CCI : 0,80 ; biais : −3,3 %). Bien que le SLG fût comparable entre QLAB 9.0 and EchoPAC 12.1 (CCI : 0,95 ; biais : 0,5 %), la concordance était plus faible entre QLAB 10.2 et EchoPAC 13.1.1 endo (CCI : 0,91 ; biais : 1,1 %), mid (CCI : 0,73 ; biais : 3,9 %) et epi (CCI : 0,54 ; biais : 6,0 %). La variabilité interobservateur de tous ces logiciels était excellente, sur un échantillon de 20 patients de l'étude avec des CCI situés entre 0,97 et 0,99.
Conclusion. — Les améliorations des logiciels de *speckle tracking* peuvent être associées à des modifications significatives des valeurs de SLG qui influencent la concordance entre constructeurs. Ces données peuvent avoir des implications cliniques importantes pour le suivi longitudinal des patients à l'aide du *speckle tracking*.

Introduction

Longitudinal strain describes myocardial deformation, the fractional change in length of a myocardial segment. Speckle tracking is a recent, largely angle-independent routine technique that has been used for the evaluation of myocardial longitudinal strain and has been validated against sonomicrometry [1—3]. Global longitudinal strain (GLS) is defined by the average of peak systolic longitudinal strain values from all left ventricular (LV) segments.

Clinical studies have demonstrated major additional diagnostic and/or prognostic values of GLS compared with conventional indices of LV systolic function in various settings, such as heart failure, valvular heart disease and cardiomyopathies [4,5]. Previous reports have demonstrated significant differences between longitudinal strain values obtained with speckle tracking using the first generation of software products released by various manufacturers [6,7]. Owing to different post-processing algorithms [7], the American Society of Echocardiography (ASE) and the European Association of CardioVascular Imaging (EACVI) set up an expert group, combining researchers and industry members, to achieve a consensus document detailing speckle tracking measurements [8,9]. As a result, reports have demonstrated an agreement between two software products from two major vendors (EchoPAC 12, GE Medical, Milwaukee, WI, USA and QLAB 9, Philips, Andover, MA, USA) [10,11]. Changes in vendor and reader can be expected to influence GLS values by up to 5% [11]. However, since the publication of these studies, upgrades of software products have been released. In addition, one software upgrade (GE EchoPAC 13.1.1) enables distinctive evaluation of endocardial, mid-myocardial and epicardial myocardial strain, hence complicating the comparison of GLS values between vendors [12]. Whether changes in these software releases influence GLS assessment remains unknown. Hence, we studied the effect of software product upgrade releases on measurement and intervendor consistency of GLS.

Methods

Study population

Patients referred for echocardiography at the echocardiography laboratory of the Saint Philibert Hospital (Lille Catholic University) during a 2-week period were screened for inclusion in the study. Inclusion criteria were: good visualization of all LV segments (allowing speckle tracking and measurement of LV GLS), sinus rhythm and consent to participate. Patients with poor echogenicity, i.e. speckle tracking not possible in at least one LV segment, were excluded. In addition, control subjects from the hospital staff with normal ECG, echocardiogram and free of any cardiovascular disease were asked to enroll in the study population.

Standard echocardiography and workflow

Transthoracic echocardiograms were acquired by experienced echocardiographers with two commercially available ultrasound transducers and equipment (M5S-D probe, Vivid E9, GE Medical; X5-1 probe, iE33, Philips) located in the same echocardiography room. Each participant underwent comprehensive assessment of cardiac anatomy and function with one of the ultrasound systems. The order of examination with the two machines was randomized. Acquisitions with both systems were performed during the same echocardiographic examination and patients remained in the same position. Sector size and depth were adjusted to achieve optimal visualization of all LV segments at the highest possible frame rate. At least three video loops of one cardiac cycle were obtained for apical views.

Speckle tracking strain echocardiography

QLAB software versions 9.0 and 10.2 were used for images obtained from Philips iE33, while EchoPAC software products 12.1 and 13.1.1 were used to analyse data obtained with GE Vivid E9. Segmental longitudinal strain values (on a 17-segment ASE model) were calculated from the three apical views obtained on each ultrasound machine and with each software package to obtain GLS (%). All acquired apical views were available for off-line quantification. GLS values were computed after having determined the onset of aortic valve closure using Doppler recordings or visual inspection of the kinetics of the aortic valve in long-axis views.

The automatic tracking of the endocardial contour was performed in end-systole with EchoPAC and in end-diastole with QLAB. Tracking was carefully verified and the region of interest was manually corrected to ensure optimal tracking and to cover the entire thickness of the LV myocardium. The multilayer two-dimensional (2D) strain speckle tracking (EchoPAC 13.1.1) starts, similarly to EchoPAC 12.1, by delineating the endocardial border; however, instead of a single chain of nodes, the myocardial wall is automatically defined with multiple chains of nodes, allowing investigation of the three myocardial layers: endocardial (endo), midwall (mid) and epicardial (epi) [12]. Longitudinal 2D speckle tracking strain values were analysed off-line by a blinded investigator (A.L.C.). The same investigator performed image analyses with both the upgrade and the former release of each software (GE or Philips). A gap of more than 2 weeks was required between reading sessions. A second investigator (S.M.) independently repeated the strain analyses to test the interobserver variability of each software in a randomly selected set of 20 echocardiograms.

Statistical analyses

Baseline data are presented as means ± standard deviations (SDs) or numbers and frequencies. For the sake of clarity, GLS has been converted into absolute values to depict comparisons as recommended by the European Association of Cardiovascular Imaging (EACVI)/ASE/Industry Task Force to standardize deformation imaging [9]. Student's t-test was used to compare mean GLS values. Intraclass correlation coefficients (ICCs) were obtained to compare GLS values between software versions, between vendors and between observers. Bland—Altman plots of differences between GLS by QLAB 9.0 versus 10.2, EchoPAC 12.1 versus 13.1.1, QLAB 9.0 versus EchoPAC 12.1 and QLAB 10.0 versus EchoPAC 13.1.1 and mean values of GLS were produced to study potential bias and to obtain 95% limits of agreement (LOA)

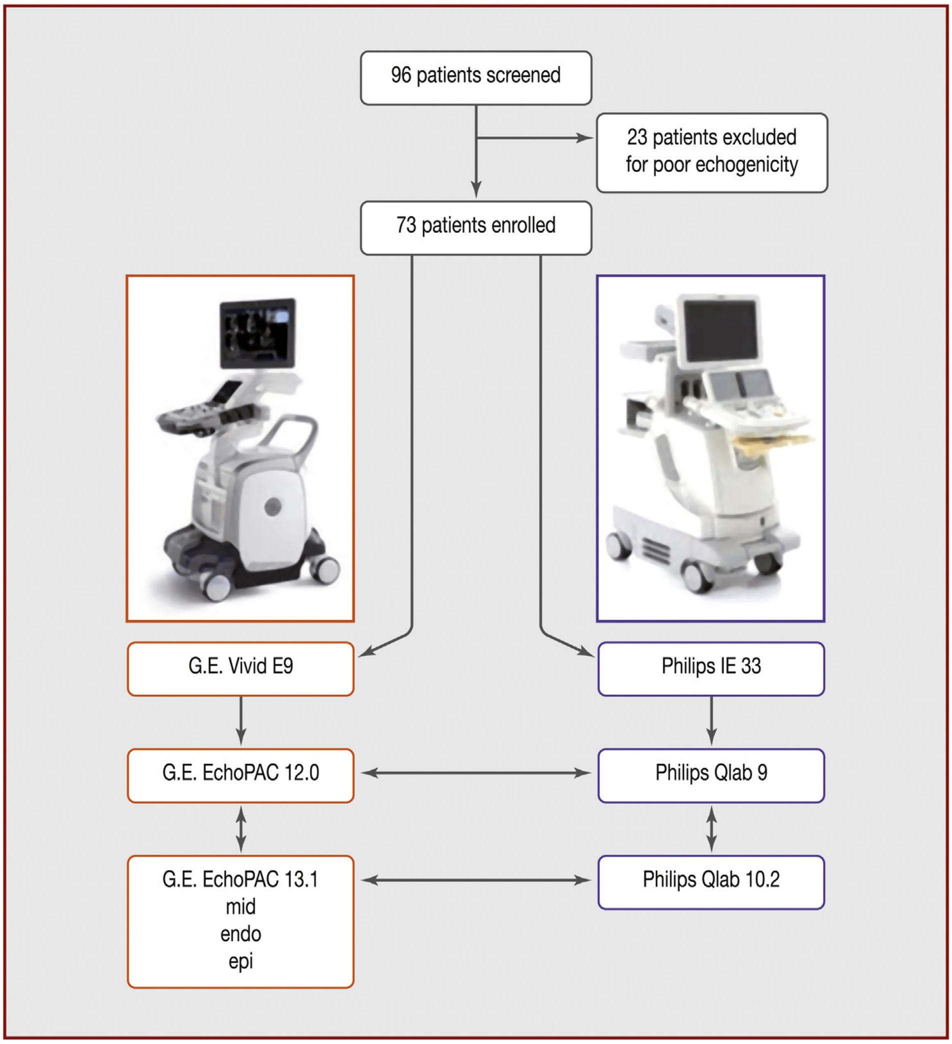

Figure 1. Flow chart of the study population.

[13]. Variations in the range of GLS values for intersoftware comparison, intervendor comparison and interobserver comparison were derived from these LOAs. Both ICCs and Bland—Altman results are reported as these methods can provide inconsistent results in agreement studies [14]. Interobserver variabilities of the software products were also evaluated using coefficients of variation (CV [%] = 100 × SD of the difference between observers/mean of the difference between observers). Two-sided P values < 0.05 were considered statistically significant. Statistical analyses were performed using PASW 18.0 (IBM, Inc., Bois-Colombes, France) and MedCalc for Windows version 12.5.0 (MedCalc Software, Mariakerke, Belgium).

Results

Of 96 subjects who were screened for inclusion in the study, 23 were excluded for poor echogenicity. Hence, the final study cohort consisted of 73 subjects (65 patients and 8 healthy volunteers) (Fig. 1). Baseline characteristics of the study population are summarized in Table 1.

Echocardiography

The mean frame rates for GE and Philips images were 62 ± 3 and 61 ± 11 frames/s, respectively. Mean LV end-diastolic and end-systolic volumes were 143 ± 60 and 74 ± 60 mL, respectively. The mean ± SD (range) LV ejection fraction was 52 ± 16% (13—77%) and LV ejection fraction was < 50% in 26 patients (36%).

Intersoftware comparison of GLS

Comparing the two QLAB versions, mean absolute GLS was higher using QLAB 10.2 versus 9.0 (|19.3| ± 5.8% vs. |17.1| ± 6.0%; bias: 2.2%; P < 0.0001) and the ICC was 0.88 (Table 2; Fig. 2A). For the EchoPAC versions, ICCs were high for the comparisons between EchoPAC 12.1 and either EchoPAC 13.1.1 endo (0.93) or EchoPAC 13.1.1 mid (0.95), but low between EchoPAC 12.1 and EchoPAC 13.1.1 epi (0.80) (Table 2). EchoPAC 13.1.1 endo GLS values were slightly higher than those using EchoPAC 12.1 (|18.2| ± 6.6% vs. |16.6| ± 5.5%; bias 1.6%; P < 0.0001; Fig. 2B). EchoPAC 13.1.1 mid GLS values were slightly lower than those derived from

Table 1 Demographic and clinical data of the study population.

	All subjects ($n = 73$)
Demographics	
Age (years)	61 ± 16
Men	43 (59)
Body mass index (kg/m^2)	26.0 ± 0.6
Diabetes	18 (25)
Hypertension	31 (42)
Smoking	15 (21)
Dyslipidaemia	28 (38)
Main echocardiography findings (patients with structural heart disease)	
Heart failure with preserved or depressed LV ejection fraction	18 (25)
Ischaemic heart disease	3 (4)
Hypertrophic cardiomyopathy	3 (4)
Significant valvular heart disease	12 (16)
Reason for echocardiography (patients without structural heart disease)	
Chest pain	8 (11)
Other[a]	21 (29)
Healthy volunteers	8 (11)

Data are expressed as mean ± standard deviation or number (%). LV: left ventricular.
[a] Hypertension, diabetes, preoperative evaluation for non-cardiac surgery or stroke.

EchoPAC 12.1 (|15.4| ± 5.5% vs. |16.6| ± 5.5%; bias: −1.1%; $P < 0.0001$; Fig. 2C). Variations in the range of GLS values owing to upgrade of the software products was 4%, except for the comparison between EchoPAC 12.1 and EchoPAC 13.1.1 mid, which was 3% (Table 2).

Intervendor comparison of GLS

The intervendor comparison of global longitudinal strain is detailed in Table 2. Comparing the two earlier software versions, the ICC between QLAB 9.0 and EchoPAC 12.1 was excellent (0.95) (Table 3). The mean GLS using QLAB 9.0 was only slightly higher than GLS using EchoPAC 12.1 (|17.1| ± 6.0% vs. |16.6| ± 5.5%; bias: 0.5%; $P = 0.03$) with 95% LOA of strain values ranging between −3.1% and +4.1% (Fig. 3A).

For the later software versions, the ICC was high between QLAB 10.2 and EchoPAC 13.1.1 endo-derived GLS (0.91). Mean GLS using QLAB 10.2 was higher than GLS using EchoPAC 13.1.1 endo (|19.3| ± 5.8% vs. |18.2| ± 6.6%; bias: 1.1%; $P = 0.0006$), with 95% LOA of strain values ranging between −4.1% and 6.4% (Fig. 3B). The ICCs were low between QLAB 10.2 and EchoPAC 13.1.1 mid or EchoPAC 13.1.1 epi (0.73 and 0.54, respectively) (Table 3). QLAB 10.2-derived GLS values were higher than EchoPAC 13.1.1 mid- and epi-derived GLS values (|19.3| ± 5.8% vs. |15.4| ± 5.5% and |13.3| ± 5.0%; biases: 3.9% and 6.0%; both $P < 0.0001$; Fig. 3C and D). Variations in the range of GLS values owing to changes in the vendor ranged from 4% to 6% (Table 2).

Interobserver comparison of GLS

As shown in Table 3, the ICCs between first and second observers were excellent for all software versions, with values ranging from 0.97 to 0.99. There was only minimal bias between the two observers (Table 3). Variations in the range of GLS values owing to changes in observer ranged from 2% to 3% (Table 3). Interobserver CVs were low for all software products, ranging from 4.2% to 6.6% (Table 3).

Discussion

The results indicate that upgrades of speckle tracking software products are associated with significant changes in GLS values. Overestimation or underestimation of mean GLS values were observed depending on the software and

Table 2 Intersoftware and intervendor comparisons of GLS data (absolute values) between QLAB and EchoPAC speckle tracking strain software products.

	ICC	Bland—Altman	
		Bias (LOA)	Variations in the range of GLS (%)
Intersoftware			
QLAB 10.2 vs. QLAB 9.0	0.88	2.2 (−1.8 to 6.3)	4
EchoPAC 13.1.1 endo vs. EchoPAC 12.1	0.93	1.6 (−1.8 to 5.0)	4
EchoPAC 13.1.1 mid vs. EchoPAC 12.1	0.95	−1.1 (−4.0 to 1.7)	3
EchoPAC 13.1.1 epi vs. EchoPAC 12.1	0.80	−3.3 (−6.6 to 0.0)	4
Intervendor			
QLAB 9.0 vs. EchoPAC 12.1	0.95	0.5 (−3.1 to 4.1)	4
QLAB 10.2 vs. EchoPAC 13.1.1 endo	0.91	1.1 (−4.1 to 6.4)	6
QLAB 10.2 vs. EchoPAC 13.1.1 mid	0.73	3.9 (−1.2 to 8.9)	5
QLAB 10.2 vs. EchoPAC 13.1.1 epi	0.54	6.0 (0.7 to 11.4)	6

GLS: global longitudinal strain; ICC: intraclass correlation coefficient; LOA: limits of agreement (95% confidence interval).

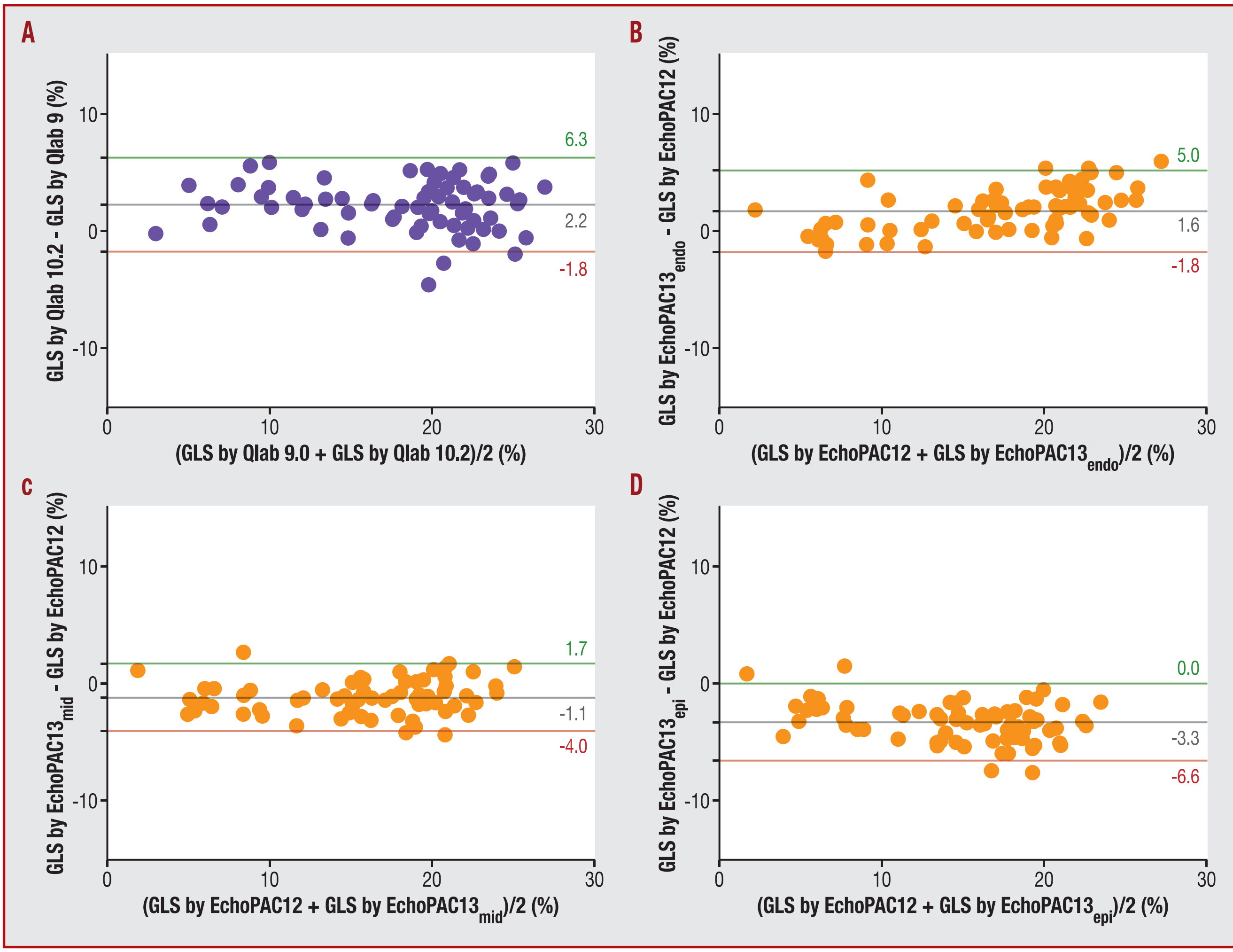

Figure 2. Bland—Altman plots of the absolute differences between GLS by A. Philips QLAB 10.2 and 9.0, B. EchoPAC 13.1.1 endo and 12.0, C. EchoPAC 13.1.1 mid and 12.0 and D. EchoPAC 13.1.1 epi and 12.0. The solid horizontal lines show the mean differences in GLS values obtained by the two software products; the dotted lines show the LOAs (95% CIs). CI: confidence interval; GLS: global longitudinal strain; LOA: limit of agreement.

myocardial layer studied (endo, mid or epi). The variation in the range of GLS owing to these changes was observed to be higher than the variation in the range of GLS due to interobserver variability (3—6% vs. 2—3%). There was also less consistency between vendors with the newer than with the former software (variation in the range of GLS 5—6% vs. 4%). This finding has important clinical implications for the longitudinal follow-up

Table 3 Interobserver comparison of GLS data (absolute values from a subset of 20 patients) between QLAB and EchoPAC speckle tracking strain software products.

	ICC	Bland and Altman		CV (%)
		Bias (LOA)	Variations in the range of GLS (%)	
QLAB 9.0	0.98	0.2 (—2.6 to 2.9)	3	5.9
QLAB 10.2	0.99	—0.3 (—2.5 to 2.0)	3	4.2
EchoPAC 12.1	0.97	1.0 (—1.5 to 3.5)	3	6.6
EchoPAC 13.1.1 endo	0.98	—0.8 (—3.0 to 1.4)	3	5.4
EchoPAC 13.1.1 mid	0.98	—0.7 (—2.7 to 1.3)	2	5.8
EchoPAC 13.1.1 epi	0.98	—0.6 (—2.5 to 1.2)	2	6.2

CV: coefficient of variation; GLS: global longitudinal strain; ICC: intraclass correlation coefficient; LOA: limits of agreement (95% confidence interval).

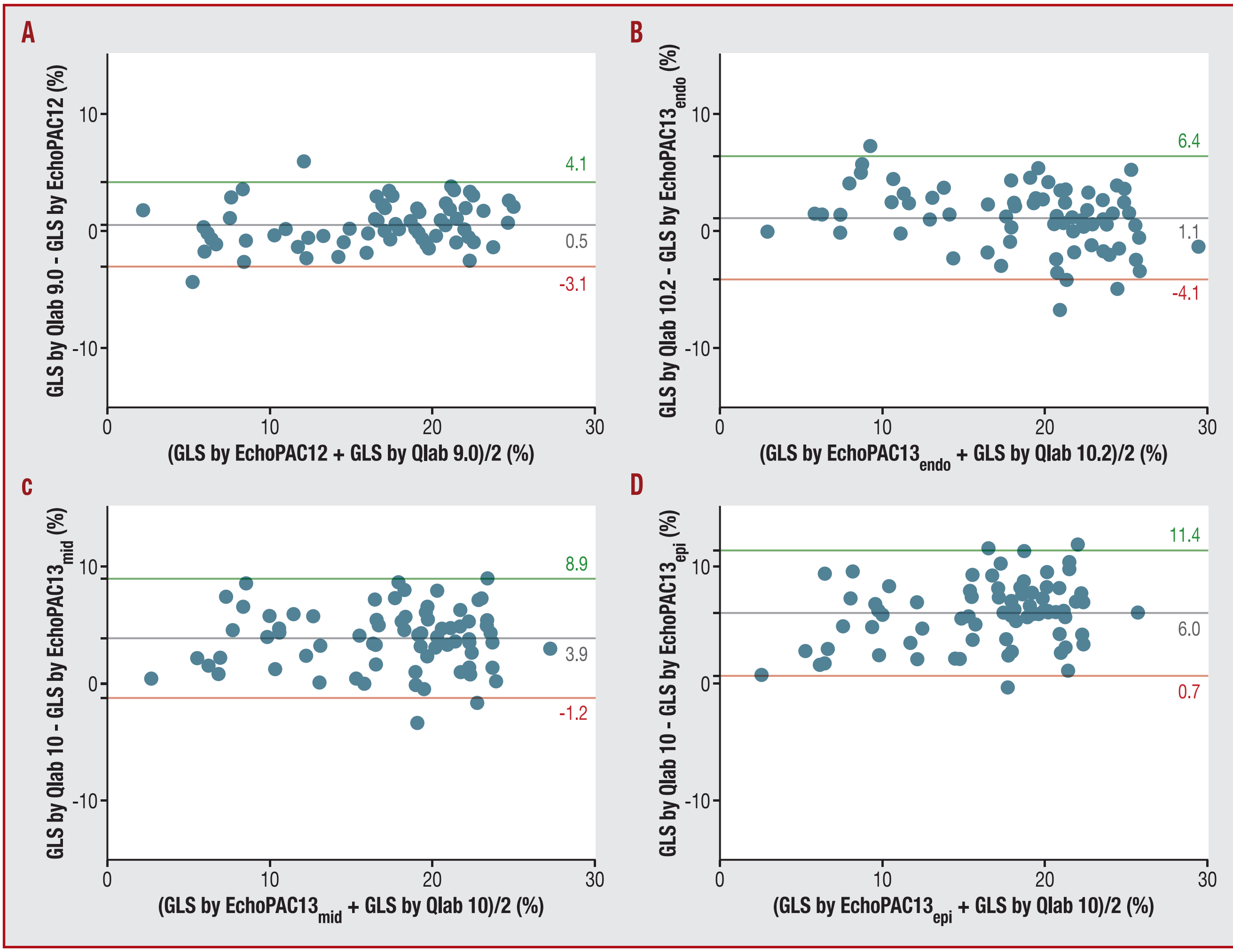

Figure 3. Bland—Altman plots of the absolute differences between GLS by A. Philips QLAB 9.0 and EchoPAC 12.1, B. QLAB 10.2 and EchoPAC 13.1.1 endo, C. QLAB 10.2 and EchoPAC 13.1.1 mid and D. QLAB 10.2 and EchoPAC 13.1.1 epi. The solid horizontal lines show the mean differences in GLS values obtained by the two software products; the dotted lines show the LOAs (95% CIs). CI: confidence interval; GLS: global longitudinal strain; LOA: limit of agreement.

of patients with speckle tracking strain echocardiography.

Although significant differences have been reported for GLS measured with early releases of speckle tracking software products (QLAB 7.0, 8.0 and EchoPAC 6.0, 11.0), we [10] and others [11] have observed very good agreement between GLS obtained with QLAB 9.0 and EchoPAC 12.1. This is due to the ASE/EACVI expert group, comprising interested researchers and industry members, reaching agreement regarding the details of what is measured by these techniques in order to reduce intervendor variability [8]. A recent consensus document of the EACVI/ASE/Industry Task Force has provided definitions, names, abbreviations, formulas and procedures for the calculation of physical quantities derived from speckle tracking echocardiography to create a common standard [9]. These guidelines say that the region of interest should be explicitly defined in terms of its spatial localization (endo, mid, epi or entire wall) [9]. Compared with QLAB 9.0, we found that QLAB 10.2 overestimated absolute GLS values; however, there was better agreement between GLS obtained at the endocardium with EchoPAC 13.1.1 and GLS obtained by QLAB 10.2. This finding is not unexpected as absolute value of longitudinal strain is highest in the endocardium and lowest in the epicardium. In line with this, absolute GLS values at the midventricular and epicardial layers with the EchoPAC 13.1.1 software were consistently lower than with those derived from QLAB 10.2. Hence, changes in software versions may be responsible for variations in GLS values, which may affect the clinical significance of quantitative differences in GLS.

These findings have important clinical implications for multi- and single-centre longitudinal studies. Numerous studies have demonstrated the clinical relevance of speckle tracking GLS in various pathologies [5], including heart failure with reduced or preserved LV ejection fraction [15,16], coronary artery disease [17] and mitral and/or aortic valve diseases [18,19]. GLS can also be used to identify subclinical disease in patients with diabetes [20] or cardiomyopathies [21]. A decrease in absolute GLS values is also an early predictor for cardiotoxicity in patients undergoing chemotherapy [22]. Deterioration in GLS over time can be used to identify high-risk patients who need closer follow-up and may benefit from specific therapies to improve their outcome. GLS can also be used to track subclinical changes in LV function over time with serial echocardiographic examinations. Therefore, consistency between serial GLS measurements is important.

Several factors may influence GLS values including changes in blood pressure [23], data acquisition, in vendor or in reader [11]. Therefore, knowing that upgrades in speckle tracking software may influence GLS values is important, in order to help to distinguish software-related from disease-related changes in GLS over time. Hence, upgrades of speckle tracking strain software products may necessitate the reanalysis of previously acquired echocardiograms in order to adequately interpret changes in GLS over time.

Limitations

Strains from short-axis views were not assessed, as radial strain cannot be obtained with Philips QLAB software. Also, because echocardiograms were performed and analysed by cardiologists with extensive experience in echocardiography and speckle tracking strain analysis, these results may not reflect broad routine practice.

Conclusions

Upgrades of speckle tracking software products may be associated with significant changes in GLS values that could affect intervendor and intersoftware consistency. This finding has important clinical implications for the longitudinal follow-up of patients with speckle tracking echocardiography.

Disclosure of interest

S.M.: Grants or consulting fees from General Electrics Healthcare and Philips Healthcare.

The other authors declare that they have no competing interest.

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